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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/937,756	09/25/1997	DAVID C. RUEGER	JJJ-P06-504	2132

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EXAMINER	
WANG, CHANG YU	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/937,756	RUEGER ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 9, 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *97,99 and 105-113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *97,99 and 105-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendments/claims

Applicant's amendment filed August 9, 2006 is acknowledged. Claims 1-96, 98, 100-104 are cancelled. Claims 97, 99, 105-111, and newly added claims 112-113 are pending in this application and under examination. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The rejections of claims 97, 99, 105-111under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of 5,656,593, claims 1-29 of 5,733,878, claims 1-14 of 6,333,312, claims 1-25 of 6,281,195, claims 1-20 of 5,972,884, claims 1-24 of 5,739,107, claims 1-19 of 5,849,686, claims 1-5 of 6,531,445, claims 1-8 of 6,399,569 and claims 1-8 of 6,936,582 have been withdrawn but for the ones indicated below. It is incumbent on the applicant to inform the office of all related subject matter and to file all related terminal disclaimers. See 37 CFR 1.56, Duty to disclose information material to patentability.

Claim Rejections/Objections Maintained

Obviousness-Type Non-Statutory Double Patenting

The rejections of claims 97, 99, 105-111under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of 6,288,031, claims 1-2 of 6,495,513, claims 1-16 of US 6,800,603, and claims 1-18 of 6,949,505 are

maintained for reasons of record in the previous office action. The rejection is also applied to new claims 112-113 since these claims recite the same limitation as in original claims.

Applicant argues that the amended claims are distinguished from the claims in the cited patents because these claims do not pertain to neuronal cells that are damaged, or are at risk of being damaged, due to chemical or physical injury or due to a neuropathy. Applicant argues that claims 1-8 of 6,288,031 pertain to extravasation of effector cells so they do not relate to neuronal cells as in the amended claims of the instant application. In addition, Applicant states that Applicant will consider filing terminal disclaimers over claims 1-18 of US 6,949,505, claims1-16 of US 6,800,603 and claims 1-2 of US 6,495,513 once patentable subject matter is identified.

Applicant's arguments have been fully considered but they are not found persuasive. The amended claims recite decreasing neuronal cell death associated with a neuropathy or injury. The neuropathy and injury include cell damage in peripheral nervous system and different tissues as described in the specification (p.3, p. 13-15). In addition, Applicant defines neuropathy as the following:

"The neuropathies, which have been identified to date, may affect the neurons themselves or the associated glial cells, may result from cellular metabolic dysfunction, infection, exposure to toxic agents, autoimmunity dysfunction, malnutrition or ischemia. In some cases the cellular dysfunction is thought to induce cell death directly. In other cases, the neuropathy may induce sufficient tissue necrosis to stimulate the body's immune/inflammatory system and the mechanisms of the body's immune response to the initial neural injury then destroys the neurons and the pathway defined by these neurons. Currently no satisfactory method exists to repair the damage caused by these neuropathies, which include multiple sclerosis, amyotrophic lateral sclerosis (ALS), Huntington's chorea, Alzheimer's disease, Parkinson's disease (parkinsonism), and metabolically derived disorders, such as hepatic encephalopathy". "....neuroprotective effects to alleviate neural pathway damage associated with the body's

immune/inflammatory response to an initial injury to nerve tissue. Such a response may follow trauma tonerve tissue, caused, for example, by an autoimmune dysfunction, neoplastic lesion, infection, chemical or mechanical trauma, disease, by interruption of blood flow to the neurons or glial cells, for example following ischemia or hypoxia, or by other trauma to the nerve or surrounding material."

The claims 1-6 of '031 encompass a method of treating injury to neural tissue and reducing inflammatory response in a patient with neural tissue damage. Applicant's instant claims to decreasing neuronal cell death associated with neuropathy and damage resulting from nerve injury merely broaden the scope of the issued claims, since they encompass damage from all causes. The claims of '513 encompass a method for promoting neurite extension and stimulating nerve gap repair, which results in promoting neuronal survival and decreasing neuronal cell death. The claims of '603 encompass a method of stimulating a neural cell adhesion molecule, which is an inherent result of administration of OP-1 or related morphogen as in Applicant's instant claims. The claims of '505 encompass a method of enhancing dendrite outgrowth, which results in promoting neuronal survival and decreasing neuronal cell death. Thus, the claimed methods in the cited patents are obvious over the instant claims and substantially overlap in scope with the instant claims. Therefore, the rejection of claims under obviousness double patenting as being unpatentable over claims 1-8 of 6,288,031, claims 1-2 of 6,495,513, claims 1-16 of US 6,800,603, and claims 1-18 of 6,949,505 is maintained of record until a terminal disclaimer is filed. It is noted that traversal at the time of indication of allowable subject matter will not be considered timely. The rejection is also applied to new claims 112-113.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 97, 99, 105-113 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of decreasing neuronal death associated with a neuropathy or injury by administering to a subject with a morphogen comprising a dimeric protein having fragments of amino acids 38-139 and 43-139 of SEQ ID NO:5 with homology as recited in claim 97, does not reasonably provide enablement for a method for decreasing neuronal cell death associated with all forms of neuropathy or injury comprising administering a morphogen to a subject afflicted with or at risk of being afflicted with a neuropathy or injury wherein the morphogen comprising any amino acid sequence of morphogens as recited in claim 97 as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

Claims 97, 99, 105-113 are directed to a method for decreasing neuronal cell death associated with a neuropathy, chemical and physical injury comprising administering a morphogen to a subject afflicted with or at risk of being afflicted with a neuropathy or chemical/physical injury.

The specification is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The claims recite administering a subject at risk of being afflicted with a neuropathy, chemical/physical injury. While the specification teaches decreasing neuronal death caused by sciatic nerve injury or optic nerve injury by OP-1, it does not provide sufficient guidance as to whether neuronal death could be decreased in all forms of neuropathy, including those caused by different diseases, chemical or physical injury by OP-1 or related morphogens. In addition, the specification fails to provide guidance as to how to

identify/predict a population being at risk of the conditions as mentioned above. Further, Applicant fails to provide any evidence as to whether administering OP-1 or related morphogens to any person at risk of a neuropathy or injury can lessen potential neuronal cell death in the person since the causes of a neuropathy or injury are very divergent. For example, Alzheimer's disease or Parkinson's disease is due to the problem of protein processing of APP or poly-Q accumulation. The causes of these diseases are not fully deciphered. In addition, most of us are at risk of developing Alzheimer's disease. Applicant fails to teach how to identify whether we are at risk of developing Alzheimer's disease. In addition, if the cause of Alzheimer's disease is due to the genetic defect in certain genes involved in the whole process of Aβ production or clearance, Applicant fails to provide sufficient guidance as to how to decrease neuronal cell death in people at risk of developing Alzheimer's disease and further decreasing neuronal death caused by the disease. Thus, it is unpredictable whether neuronal cell death could be decreased in all forms of neuropathy, including those caused by different disease, chemical, or physical injury by administration of OP-1 or related morphogens since the causes are divergent and unpredictable. It is also unpredictable whether it is predictable to lessen potential neuronal cell death in a person being "at risk" by administering these morphogens to him/her since we don't know how to identify a population that is "at risk" of these conditions. The specification does not enable the broad scope of the claims. Thus, in view of the necessity of experimentation, the limited working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification, it would require more undue experimentation to practice the claimed

invention.

Conclusion

NO CLAIM IS ALLOWED.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
October 19, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER